201-14167

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Subject: Environmental Defense comments on phenethyl alcohol (PEA)

(Submitted via Internet 12/24/02 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and tadams@therobertsgroup.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for phenethyl alcohol.

The test plan for phenethyl alcohol (PEA) was prepared by the Flavor and Fragrance High Production Volume Consortia, which is comprised of 13 member companies. PEA is used as a fragrance ingredient in a number of products including cosmetics, soaps and detergents. It is also found naturally in a number of foods. Although the test plan was well organized and written, we have some concerns and we disagree with the sponsor's conclusion that no additional testing is required.

The sponsor states that greater than 99% of oral intake of PEA occurs through consumption of food containing naturally occurring PEA. This assertion is misleading based on the information contained in the test plan. The sponsor states that 700,000 kg of PEA is consumed annually as a natural component of foods while 12,500 kg are added as a flavor ingredient. However, 400,000 kg of PEA is used in cosmetics, soaps and detergents. Since PEA is almost completely absorbed following dermal application, significant internal human exposure occurs through the dermal route. Using the above figures, one can estimate that 30-40% of human exposure to PEA occurs as a consequence of its direct addition to consumer products. This estimate is consistent with some recent studies released by the CDC which revealed much higher levels of the flavoring ingredient, methyleugenol, in random blood samples than would have been predicted by the amounts added to foodstuffs.

The sponsor contends that no additional studies are needed to fulfill HPV requirements. We agree with the sponsor with two exceptions.
1. While some information is available for in vitro genetic toxicity, it is not as extensive as would be desirable particularly in light of the lack of in vivo genetic toxicity studies on PEA. Accordingly, we recommend that in vitro cell transformation studies be conducted on PEA. (The sponsor claims that data from in vivo studies on PEA metabolites can be used as a surrogate. However, this claim is not adequately justified as it is well known that metabolites often have vastly different toxicological properties than the parent compound.) If those cell transformation studies are positive, this would suggest the need for post-HPV in vivo genetic toxicity tests on PEA.
2. The sponsor proposes to use an existing repeat dose study on PEA that was conducted via the dermal route to fulfill HPV requirements for this endpoint. While the rapid and near complete absorption of PEA following

dermal application is consistent with the sponsor's proposal, we are concerned with the adequacy of this study. It was not conducted under GLP conditions and there is no evidence from the robust summary that complete histopathology was done. The study seemed to focus on ocular sensitivity. Unless the sponsors are able to provide additional histopathology results and information assuring reliability of the prior study, a repeat dose study should be conducted. While it would be scientifically appropriate to use either a dermal or an oral exposure protocol, for reasons of animal welfare an oral route is probably preferable.
3. There are no reproductive studies on PEA but there are numerous developmental toxicity studies in multiple species and using multiple routes of administration. All these studies were negative so we agree with the sponsor that no new reproductive studies need to be conducted on PEA.

Thank you for this opportunity to comment.

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